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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/319,736	08/02/1999	ELISABETH WOLPERT	000500-182	3510

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 12/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/319,736	WOLPERT ET AL	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *November 1, 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *148-158,160,161,163 and 164* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *148-158,160,161,163 and 164* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The finality of the Office action of May 3, 2006 is withdrawn in light of the rejections below.

Claims 143-147, 159 and 162 have been canceled. Claims 148-158, 160, 161, 163 and 164 are pending and under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The rejection of claims 155-157, 160, 161, 163 and 164 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained for the following reasons of record. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 157 is drawn to a composition comprising cells isolated according to the method of claim 148. Claim 160 is drawn to cells isolated according to the method of claim 148, antigens or epitopes expressed by said cells. Claim 161 is drawn to a composition comprising immunological effector cells isolated according to the method of claim 155 and claim 164 is drawn to a composition comprising effector cells isolated by the method of claim 163. It is noted that claims 157 and 160 are dependent upon the cell isolated by the method of claim 148; the methods of claims 155 and 156 depend on the cells isolated by the method of claim 148, and that claim 161 is a method reliant on the identity of cell isolated by the method of claim 155, which in turn is reliant on claim 155 which is drawn to a process comprising stimulating isolated immunological effector cells in vitro with cell isolated according to the method of claim[s] 148. The products of claims 157, 160, 161 and 164 lack adequate written description, because the specification cannot adequately describe cells which have yet to be isolated. It logically follows that if a product itself is not adequately described, the method o f using said product cannot be adequately described.

Applicant argues that the process comprises a novel intermediate material that is defined by its method of manufacture. This is not the fact pattern of the instant claims. The products are immunological effector cells that selectively recognize cells showing impaired cellular peptide processing for MHC presentation. The "method of manufacture" does not provide a control for the entire phenotype of the isolated cells which results from the impaired MHC presentation. Given the instant method, one of skill in the art could not anticipate how the impaired processing for MHC presentation in the cell will result in a recognition of an undescribed TAP-independent epitope by a CTL (Example 2, page 24). One of skill in the art cannot anticipate if a particular of peptide or peptides, degraded by an alternative mechanisms, will be presented in the MHC cleft in lieu of the peptides which are processed by TAP-dependent processing. Thus, it logically follows that the effector cells which selectively recognize cells with impaired peptide processing are determined by selection based on the peptides which are ultimately displayed by the MHC-processing impaired cells. Said effector cells are not adequately described because the cells isolated by the method of claim 148 are themselves not adequately described.

Claims 148-157, 160, 161, 163 and 164 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of target cells with an effective dose of a substance that impairs cellular peptide processing for MHC presentation and the isolation of cells which activate CTL that selectively recognize cells showing endogenous epitopes associated with impaired cellular peptide processing for MHC, wherein the cells which are treated are not professional antigen presenting g cells, does not reasonably provide enablement for the treatment of professional antigen presenting cells with an effect dose of a substance that impair cellular processing for MHC presentation and isolation of CTL which selectively recognize cells showing endogenous peptides associated with impaired cellular peptide processing for MHC presentation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification states that the cells may be chosen from hematopoietic cells, especially dendritic cells, and that the cells can be healthy cells from an affected tissue or organ (page 10, lines 9-13), which includes cells which are not professional APC. However, the specification

then teaches that CTL recognition requires the presence of MHC molecules and the absence of TAP in the target. In the case of choosing dendritic cell to be contacted with the substance that inhibits or eliminates TAP, the dendritic cell would not be able to function as an effector cell for antigen presentation, because the dendritic cell relies on a high level of expression of MHC peptides and co-peptides in the context of T-cell receptor activating ligands. Further, the dendritic cell would then be reminiscent of the target. The altering of the plurality of MHC peptides displayed by dendritic cell would alter the T cell receptors which would be complementary to the displayed dendritic cell antigens. There is no evidence in the specification or any art of record to suggest that the limiting the CTL activated by the dendritic cell will provide CTL which recognize the TAP deficient antigen on the target cells

Claim 158 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. claim 158 requires the administration to a mammal immunological effector cells which selectively recognize cell showing impaired cellular peptide processing for MHC presentation. The specification teaches that the TAP deficient cell line RMA-S can elicit CTL which recognize the non-TAP deficient tumor cell liens of RMA, El-4, Radiation Leukemia virus induced ALC, 26E-1 and p815 cells transfected with H-2K. The specification has not provided evidence that the antigen recognized by the CTL generated against the TAP-deficient variant of RMA is a universal tumor antigen, nor does the specification provide any evidence that a an immunological effector cell which selectively recognized cells showing impaired cellular possessing would be efficacious in vivo. It is noted that the presence of CTL in vivo does not correspond to treatment efficacy. Ohlen et al (Journal of Immunology, 2001, Vol.166, pp. 2863-2870) teach that T-cells recognizing normal proteins expressed in tumors can be isolated in vitro, but that the existence of said T-cells does not preclude in vivo anergy induction and deletion (page 2863, second column, lines 1-6 of the last paragraph). Antoinia et al (International Immunology, 1995, Vol. 7, pp. 715-725) teach that T-cells which are impaired in the ability to proliferate in response to antigen and unable to reject tumors in vivo were fully functional as CTL lymphocytes in vivo (page 724, first column, first

full paragraph). Yu and Restifo (Journal of Clinical Investigation, 2002, Vol. 110, pp. 289-294, especially page 292) teach that even when increased anti-tumor T-cell precursors have been induced by vaccination, the clinical response is partial and transient and most patients eventually succumb to progressively growing tumors. These references serve to demonstrate that the lysis of target cells expressing the epitope associated with TAP deficiency in vitro does not constitute evidence that said T-lymphocytes would be effective at lysing tumor cells or other undesirable cells in vivo. When given he broadest reasonable interpretation, claim 158 encompasses the treatment of a human or domestic animal in need thereof comprising the administration of immunological effector cells which recognize cells showing impaired cellular peptide processing for MHC presentation, and the scope of enablement set forth is not commensurate with the scope of the claim. It is further noted that the effector cells used in claim 158 require their isolation, such as by the method of claim 155, which would require one of skill in the art to carry out the method of claim 148 followed by the method of claim 155. Thus, one of skill in the art would be subject to undue experimentation in order to carry out the claimed method because it would not be possible to make and use the method of claim 158 without first carrying out the method of claim 148 followed by the method of claim 155.

All other rejections and objections as set forth or maintained in a previous Office action are wtihdrawn.

All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Karen A. Canella, Ph.D.
11/27/2006

KAREN A. CANELLA, PH.D
PRIMARY EXAMINER